Deutsche Menopause Gesellschaft e.V.

FIRST TO KNOW

EARLY MENOPAUSE AND PREMATURE OVARIAN FAILURE ASSOCIATED WITH INCREASED RISK OF DEMENTIA

Schweizerische Gesellschaft für Gynäkologische Endokrinologie, Kontrazeption und Menopause

NEWSLETTER APRIL 2024

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Early menopause and premature ovarian insufficiency are associated with increased risk of dementia: A systematic review and meta-analysis of observational studies.

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BACKGROUND

Many beneficial effects of oestrogens on nerve cells have been demonstrated in preclinical studies. For example, they have been shown to support the ability of neurons to communicate with each other and to regulate genes that influence neuronal survival, differentiation, regeneration and plasticity. There are therefore concerns that a premature loss of oestrogen could have a negative impact on cognition and increase the risk of dementia in women.

SUMMARY

The aim of this systematic review and meta-analysis was to investigate the association between natural or surgical early menopause (EM) or premature ovarian insufficiency (POI) and the risk of dementia [1]. EM is defined as the onset of menopause between 40 and 45 years of age (prevalence approximately 5-10%). POI is defined as the onset of menopause before the age of 40 (prevalence about 1%). Only English-language studies (cohort, case-control and cross-sectional studies) comparing women with EM/POI and women of normal menopausal age (>45 years) were included. Studies that did not have a control group or included premenopausal and perimenopausal women were excluded. Trials with women with genetic syndromes (e.g. Turner syndrome) or endocrinopathies such as PCOS were also excluded. The outcome was dementia, regardless of cause or pathogenesis.

Associations were expressed as odds ratios (OR) with 95% confidence intervals (CI). The I2 index was used to assess heterogeneity. Study quality was assessed using the Newcastle-Ottawa scale. A comprehensive literature search was conducted in databases up to August 2022. Eleven trials with a total of 4,716,862 participants were included in the meta-analysis. The meta-analysis showed a higher risk of dementia in women with EM compared to women with menopause at "normal" age (OR 1.37; 95% CI 1.22-1.54; I2 93%). Subgroup analysis by type of menopause (surgical or natural) showed an increased risk of dementia only in women with natural EM (OR 1.61, 95% CI 1.30-2.00; I2 92%). An increased risk of dementia was also found in women with POI (OR 1.18; 95% CI 1.15-1.21; I2 0%). Subgroup analyses according to HRT use, educational level, chronic diseases, smoking, alcohol consumption, exercise, diet, and number of pregnancies were not performed because the included studies did not provide extractable data.

CONCLUSION

This meta-analysis suggests that EM and POI may be associated with an increased risk of dementia. The results must be interpreted with caution due to the high heterogeneity and limited number of studies. In addition, there were no randomised controlled trials (RCTs). The important

question of whether HRT can prevent the development of dementia remains unanswered. The current position paper of the North American Menopause Society (NAMS) states that in the absence of clear evidence, HRT is not recommended at any age for the prevention or treatment of cognitive decline or dementia (Level I) [2]. There is therefore an urgent need for studies to investigate the influence of HRT on the risk of dementia in women with EM or POI. However, it remains the case that HRT is indicated in women with EM and POI to prevent other chronic non-communicable diseases, such as osteoporosis or cardiovascular disease.

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Early menopause and premature ovarian insufficiency are associated with increased risk of dementia: A systematic review and meta-analysis of observational studies.

Maturitas, 2023. 176: p. 107792.

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